



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,003	01/05/2001	Kevin C. Eggan	0399.2015-002	4649

21005 7590 08/27/2003

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER

SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
----------	--------------

1636

17

DATE MAILED: 08/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/755,003

Applicant(s)

EGGAN ET AL.

Examiner

Daniel M Sullivan

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4,5,7,9,10,12-14,17,18,20,22,24-27,29-35 and 37-48 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,4,5,14,17,18,20,27,29,30,35,37,41-44 and 46-48 is/are allowed.
- 6) ☒ Claim(s) 7,9,10,12,13,22,24-26,31-34,38-40,45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 14.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

Art Unit: 1636

DETAILED ACTION

This Non-Final Office Action is a response to the "Amendment B" filed 18 June 2003 (Paper No. 15) in reply to the Non-Final Office Action mailed 16 December 2002 (Paper No. 13). Claims 1-48 were considered in Paper No. 13. Claims 2, 3, 6, 8, 11, 15, 16, 19, 21, 23, 28 and 36 were canceled and claims 1, 4, 5, 7, 9, 10, 12, 14, 17, 18, 20, 22, 24, 25, 27, 29, 35, 37, 41, 44 and 47 were amended in Paper No. 15. Claims 1, 4, 5, 7, 9, 10, 12-14, 17, 18, 20, 22, 24-27, 29-35 and 37-48 are pending and under consideration.

Response to Amendment

Rejection of claims 2, 3, 6, 8, 11, 15, 16, 19, 21, 23, 28 and 36 is rendered moot by cancellation of the claims.

Double Patenting

Provisional rejection of claims 1-48 under 35 U.S.C. 101 as claiming the same invention as that of claims 1-48 of copending Application No. 09/957,659 is withdrawn.

Claim Rejections - 35 USC § 112

Rejection of claims 1, 5, 14, 18, 21, 40, 41 and 44 under 35 U.S.C. § 112, first paragraph, as lacking enablement for the full scope of the claims is withdrawn.

Claims 9, 10, 12, 13, 22, 24-26, 31-34, 38 and 39 stand rejected and claim 45 is newly rejected under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the

Art Unit: 1636

claimed subject matter for reasons of record and herein below in the response to arguments.

Please note: Although the enablement rejection was not previously made against claim 45, the claim is clearly directed to subject matter that is not enabled for the same reasons as indicated for claims 9, 10, 12, 13, 22, 24-26, 31-34, 38 and 39. Therefore the rejection set forth in Paper No. 13 is hereby applied to claim 45.

Claim 40 stands rejected under 35 U.S.C. 112, first paragraph, as lacking enablement for reasons of record and herein below in the response to arguments.

Rejection of claims 1, 4, 9, 22 and 41 under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claims is withdrawn.

Rejection of claims 20, 25, 26 and 47 under 35 U.S.C. 112, second paragraph, as indefinite is withdrawn.

Claim Rejections - 35 USC § 102

Rejection of claims 1, 9, 10, 12, 14, and 22 under 35 U.S.C. 102(b) as anticipated by Wang *et al.* (1997) is withdrawn in view of the limitation of the claims to using non-inbred pluripotent ES cells.

Rejection of claims 1, 14, 27, 35 and 41 under 35 U.S.C. 102(b) as anticipated by Ueda *et al.* (1995) *Exp. Anim.* 44:205-210 as evidenced by Yagi *et al.* (1993) *Anal. Biochem.* 214:70-76

Art Unit: 1636

is withdrawn in view of the limitation of the claims to a method comprising injection of non-inbred pluripotent ES cells into tetraploid blastocysts.

Claims 9, 22, 33, and 38 stand rejected under 35 U.S.C. 102(b) as anticipated by Ueda *et al.* (1995) *Exp. Anim.* 44:205-210 as evidenced by Yagi *et al.* (1993) *Anal. Biochem.* 214:70-76 for reasons of record and herein below in the response to arguments.

Claim Rejections - 35 USC § 103

Rejection of claims 18, 25, 27, 35 and 45 under 35 U.S.C. 103(a) as unpatentable over Uchida *et al.* (1995) *Anim. Sci. Technol.* 66:361-367 as evidenced by Yagi *et al.* (*supra*) in view of either one of Ueda *et al.* (*supra*) or Wang *et al.* (*supra*) is withdrawn.

In response to the rejection, Applicant argues persuasively that Ueda *et al.* teach away from using tetraploid morulae as a routine method for production of mutant mice (page 21, first full paragraph). Furthermore, the teachings of Wang *et al.* regarding to application of tetraploid blastocyst injection for the production of mice, which were relied upon for motivation to combine the teachings of the art, are equivocal. Although the concluding paragraph in the discussion section expresses enthusiasm for tetraploid blastocyst injection for the generation of mice, other statements in the discussion indicate that the method is unreliable. In particular, Wang *et al.* teaches "this technique cannot, at present, replace conventional diploid blastocyst injection for routine generation of mutant mouse strains because of the observed inefficient postnatal development of ES mice" (page 143, column 1, first full paragraph). Thus, when viewed as a whole, the teachings of the art do not provide motivation to combine the teachings of

Art Unit: 1636

Uchida *et al.* with the teachings of Ueda *et al.* or Wang *et al.* Therefore, the claimed invention would not have been obvious to one of ordinary skill in the art at the time the invention was made.

New grounds for rejection are set forth herein below.

Response to Arguments

Claim Rejections - 35 USC § 112

Claims 9, 10, 12, 13, 22, 24-26, 31-34, 38 and 39 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *wild-type* or XO mouse produced by a method wherein pluripotent ES cells are introduced into a tetraploid blastocyst of a mouse under conditions that result in production of an embryo and the resulting embryo is transferred into a foster mother which is maintained under conditions that result in development of live offspring, or a *wild-type* or XO embryo produced from a mouse tetraploid blastocyst having incorporated therein mouse non-inbred ES cells, does not reasonably provide enablement for any and all mice produced according to the methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

In response to the rejection of record, Applicant cites several teachings in the specification and art which the skilled artisan could rely upon for guidance as to how to make the claimed invention. These arguments have been fully considered but are not found persuasive because while it is acknowledged that making mutant mice is routine in the art and the

Art Unit: 1636

specification teaches how to make mutant mice by tetraploid blastocyst injection, the skilled artisan would not be able to use the full scope of the claimed invention without engaging in undue experimentation. Applicant is claiming a wide variety of mice made by the disclosed method regardless of the genotype of said mice. Therefore, the teachings of the specification and prior art must provide a patentable (i.e., specific, substantial and credible) and enabled utility for all mice regardless of the genotype. However, for reasons set forth in previous Office Actions, the phenotype arising from any given genotypic modification is highly unpredictable and, in many cases, not apparent without considerable experimentation. Given that blind trial and error experimentation would be required to uncover a useful phenotype in many, if not most, of the mice comprising mutations in each of the tens of thousands of mouse genes, the skilled artisan would not be able to use the full scope of the claimed invention without first engaging in undue experimentation.

With regard to the teachings of Sigmund and Wall, cited by the examiner as evidence for the unpredictability of phenotype arising from genetic modification, Applicant argues, "the reference does not conclude that mice and mouse embryos cannot be produced as described in the subject application or provide evidence that would lead one skilled in the art to conclude that Applicants' claimed invention is unbelievable" (page 9). This argument has been considered but is not found persuasive because the basis for the rejection is not that the claimed invention is unbelievable but that the skilled artisan would not be able to use the full scope of the claimed invention without having to engage in undue experimentation.

Applicant states, "Sigmund provides strategies to minimize genetic variation and, as such, phenotypic variation, and indicates that a common sense approach provides a framework to

Art Unit: 1636

identify the causes of phenotypic variation.” This argument is not persuasive because the teachings of Sigmund regarding minimizing genetic variation are directed to designing control experiments to assess the contribution of epigenetic effects of unlinked loci on the observed phenotype. Sigmund is relied upon to support the Examiner’s contention that the phenotype arising from any given genotypic manipulation is unpredictable. The fact that Sigmund supports this contention is further evidenced by the teachings cited by Applicant directed to identifying the causes of phenotypic variation.

With regard to the teachings of Doetschman, Applicant argues that the teachings therein do not support the Examiner’s conclusion that a phenotype arising from any given mutation or genetic manipulation of a transgenic mouse is highly unpredictable. This statement seems at odds with Applicant’s own characterization of the teachings of Doetschman. Applicant states, “[Doetschman] provided possible reasons for unexpected knockout phenotypes and strategies for interpreting unexpected knockout phenotypes and for dealing with apparent lack of knockout phenotypes” (bridging pages 9-10, emphasis added). It would seem that if the phenotype arising from any given mutation or genetic manipulation were predictable, there would be no need for explanation of unexpected phenotypes, or strategies for dealing with unexpected phenotypes or the apparent lack of phenotype. Clearly, the fact that Doetschman is teaching strategies to deal with the unpredictability of phenotype is evidence for said unpredictability.

Next, Applicant asserts, “the need for empirical experimentation to determine a phenotype is not a sufficient basis to question the enablement provided in the specification, particularly since such experimentation is routine in the art” (page 10). Applicant then describes in general terms the types of assays that can be performed to determine the phenotype of a

Art Unit: 1636

mouse. However, as the utility of the claimed invention requires that the skilled artisan know the phenotype of the mouse, Applicant's arguments amount to an invitation to the skilled artisan to experiment to discover how to use the claimed invention. Applicant is reminded, "[l]aw requires that disclosure in application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use for themselves" (*In re Gardner, Roe and Willey* 166 USPQ 138).

Next, Applicant argues that the skilled artisan would know how to use any mutant mouse because "[t]he specification teaches that the mutant mouse model serves as a model of a condition that occurs in a different mammalian species" (page 12). This argument is not found persuasive because the claims are not limited to mice which can serve as a model of a condition that occurs in a different mammalian species. Applicant is claiming *all* mice made by the disclosed methods regardless of genotype or phenotype. As pointed out in Paper No. 13, Doetchman teaches that it is not uncommon for a genetically engineered mouse to have no apparent phenotype (page 137, paragraph 1). Clearly the skilled artisan would not know how to use a mouse having no apparent phenotype. Furthermore, not all phenotypes would be useful disease models. For example, it is conceivable that one of the mice claimed by Applicant has no phenotype other than that the mouse fails to grow whiskers, or perhaps has a short tail. Again, the skilled artisan would clearly not know how to use such an animal.

Thus, for reasons of record, claims 9, 10, 12, 13, 22, 24-26, 31-34, 38 and 39 stand rejected and claim 45 is newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *wild-type* or XO mouse or embryo produced according

Art Unit: 1636

to the disclosed methods, does not reasonably provide enablement for the wide variety of mice produced according to the methods.

Claim 40 was rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to the rejection of record, Applicant argues that it is within the skill of the skilled artisan at the time the subject application was filed to determine the phenotype of a mouse produced using the methods described in Applicants' specification. Applicant then describes various ways of determining phenotype. However, as stated above, because the utility of the claimed invention requires that the skilled artisan know the phenotype of the mouse, Applicant's arguments amount to an invitation to the skilled artisan to experiment to discover how to use the claimed invention. Again Applicant is reminded, "[I]aw requires that disclosure in application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use for themselves" (*In re Gardner, Roe and Willey* 166 USPQ 138). Therefore, for reasons of record in Paper No. 13 and herein above, the disclosure is not enabling for claim 40.

Claim Rejections - 35 USC § 102

Claims 9, 22, 33, and 38 were rejected under 35 U.S.C. 102(b) as anticipated by Ueda *et al.* (1995) *Exp. Anim.* 44:205-210 as evidenced by Yagi *et al.* (1993) *Anal. Biochem.* 214:70-76.

In response to the rejection of record, Applicant has amended the method claims such that they are limited to introducing non-inbred pluripotent ES cells into tetraploid blastocysts by

Art Unit: 1636

injection. Applicant argues that Ueda *et al.* do not teach or suggest producing mice by injection of non-inbred pluripotent ES cells into tetraploid blastocysts. However, claims 9, 22, 33 and 38 are product by process claims and as such reads on a mouse produced from non-inbred ES cells using tetraploid embryos by any means. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) states: “[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” Ueda *et al.* teaches production of mice from non-inbred ES cells by aggregation with tetraploid morulae, which mice would be entirely derived from said non-inbred ES cells. Although Ueda *et al.* teaches a different method of combining the ES cells with the tetraploid embryo, the skilled artisan would not expect that the mouse produced by aggregation of ES cell with a tetraploid morulae would be different from a mouse produced by injection of ES cells into a tetraploid blastocyst. Thus, absent evidence to the contrary, the mouse produced by the method of Ueda *et al.* anticipates the mouse of the instant claims.

New Grounds

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1636

Claims 9, 10, 12, 13, 22, 24-26, 31-34, 38-40 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

The claims are directed to mice and embryos produced according to the methods disclosed in the instant application and to a method of using said mice to identify a drug to be administered to treat a condition in a mammal. The specification teaches that the ES cells used in the methods, and thus the mice produced thereby, contain at least one/one or more genetic alterations or mutations or can be non-mutant. The specification also provides non-limiting examples of mutations that can be present in non-inbred ES cells including “transgenes, targeted or random mutations, conditional mutations, targeted insertions of foreign genes, YAC and BAC sized transgenes, all or part of a chromosome, which may be from the same species as the embryo or another species, such as from a human. They include physical knockout of all or part of a gene, functional knockout of a gene, introduction of a functional gene and introduction of DNA or a gene portion that changes the function/level of expression of a gene present in the ES

Art Unit: 1636

cell” (page 8). Therefore, the claims encompass a broadly divergent genus of mice and embryos comprising a wide variety of genetic modifications and a method of using said mice.

The Guidelines for Written Description state “when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus”, “In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus” (Federal Register, Vol. 66, No. 4, Column 3, page 1106). For reasons that are set forth in detail in previous Office Actions and herein above regarding enablement for the claims, the phenotype arising from any genetic modification in an animal is highly unpredictable. Thus, to demonstrate possession of the full genus of mutant mice encompassed by the claims it is incumbent upon Applicant to describe a sufficient number of species of said genus, both genotypically and phenotypically, such that the species described adequately reflect the variation within the genus.

The instant disclosure provides guidance as to how to make mice comprising mutations and reduction to practice of the method to produce non-mutant mice obtained using various ES cell lines. However, these examples are far from representative of the tremendously broad genus encompassed by the claims, which includes mice comprising an unlimited variety of genotypes and phenotypes. In the absence of representative species, the written description requirement for a claimed genus may be satisfied by disclosure of the relevant characteristics that identify the genus (see MPEP 2163 (ii)). In the instant case, the claims encompass such enormous breadth that it would not be possible to identify non-trivial characteristics that are even common to the entire genus, let alone features that are sufficiently characteristic that they would serve to identify the members of the genus over its full scope. Furthermore, there is nothing in the

Art Unit: 1636

disclosure that would allow the skilled artisan to envision the phenotypic characteristics of even mice comprising mutations of well characterized genes because, as established in previous office actions, phenotype is unpredictable.

Although the specification stipulates, “[i]n particular embodiments, mutant non-human mammals (e.g., mutant mice) are produced to mimic or serve as a model for a condition...that occurs in another species” (paragraph bridging pages 3-4), the disclosure fails to provide descriptive support for even these relatively limited embodiments. As the specification provides no description of which genotypes might produce a mouse that could mimic or serve as a model for a condition, the limitation to a given phenotype amounts to a claim based on function alone. An adequate written description of a mouse requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the mouse itself. It is not sufficient to define mouse solely by its phenotype, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any mouse with that phenotype. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all mice that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

Finally, with respect to claim 40, adequate description of the methods first requires an adequate description of the materials, i.e. specific mouse, which provide the means for practicing the invention.

Art Unit: 1636

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of mice produced according to the disclosed methods. Therefore, only the mice reduced to practice meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is indefinite in its recitation of “non-human tetraploid blastocyst” in line 2. As the tetraploid blastocyst of the base claim 5 is limited to a mouse tetraploid blastocyst, there is insufficient antecedent basis for non-human tetraploid blastocysts other than mouse.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1636

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10, 12, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Ueda *et al.* (1995) *Exp. Anim.* 44:205-210 as evidenced by Yagi *et al.* (1993) *Anal. Biochem.* 214:70-76.

The claims are directed to mice and mouse embryos produced according to the methods disclosed in the application. As the claims are product by process, the claims read on the products made by any means (*Id.*) and are rejected for the reasons set forth in Paper No. 13 and herein above regarding anticipation of claims 9, 22, 33 and 38. Although Ueda *et al.* teaches a different method of combining the ES cells with the tetraploid embryo, the skilled artisan would not expect that the mouse produced by aggregation of ES cell with a tetraploid morulae would be different from a mouse produced by injection of ES cells into a tetraploid blastocyst. Thus, absent evidence to the contrary, the mouse and embryos produced by the method of Ueda *et al.* anticipates the mouse and embryos of the instant claims.

Allowable Subject Matter

Claims 1, 4, 5, 14, 17, 18, 20, 27, 29, 30, 35, 37, 41-44 and 46-48 are allowed.

Claim 7 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.

Conclusion

Art Unit: 1636

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448.

The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER